Both Liver Parenchymal and Non-Parenchymal Cells Express JCAD Proteins under Various Circumstances

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In XX issue of Clin Mol Hepatol, Dr. Byoung Kuk Jang from the Department of Internal Medicine, Keimyung University School of Medicine, Daegu, Korea, provides an editorial\(^1\) to summarize major findings of our publication in the same issue\(^2\). All authors appreciate the positive comments to this original article. Regarding JCAD expression in other cell types involved in cholestatic insults, the authors would provide additional evidence to clarify this concern.

As demonstrated in the publication, JCAD is expressed in hepatic stellate cells (HSCc), which are the critical effector cell type for cholestatic fibrosis through Hippo-YAP signaling pathway. Bile epithelial cells (BECs) are often damaged, and remaining cells may proliferate to respond to cholangiocyte injury and develop bile duct reaction. This repair process is essential for maintenance of the bile duct integrity. Proliferative bile duct cells may release cytokines and other intermediates to portal fibroblasts and HSCs to coordinate the repairing process. Therefore, it is of great interest to investigate whether JCAD participates in the proliferation of BECs. In series sections of primary biliary cholangitis (PBC), immunohistochemical staining shows that bile duct epithelial cells are CK-19-positive, and JCAD is also positive in the structure of newly formed bile ducts in the same location. Moreover, transcription factor YAP is positive in some bile duct structures. In contrast, very faint staining in the portal triads was visualized in the control sections (Fig. 1). This piece of preliminary evidence demonstrates that JCAD is highly expressed in reactive bile duct epithelial cells, and presumably may contribute to their proliferative response in the same underlying mechanism. In fact, the author’s team has acquired other preliminary data to support that CK-19-positive cells are overlapped with JCAD-positive in mouse models of cholestatic insults in an on-going project. In addition,
JCAD was co-localized with F-actin in bile canaliculi in regenerative mouse liver, which implies that JCAD functions as a conjunction protein critical for the formulation of tight conjunction between hepatocytes. As a conjunction protein, it is unsurprising to demonstrate that JCAD is positive for liver sinusoidal endothelial cells (JCAD) in an on-going project. Whether inflammatory cells, such as Kupffer cells, macrophages or lymphocytes express JCAD needs further investigation. In summary, so far, the author’s team has demonstrated that JCAD is expressed in hepatocytes, bile duction epithelial cells and hepatic stellate cells under different conditions and will further investigate its role in various modes of chronic injury and repairing processes. Hopefully in-depth investigation of this novel protein would facilitate to develop new molecular therapeutics for chronic injury, which may advance to hepatic fibrosis, end-stage liver disease and malignancies.
References:


Fig. 1. JCAD was highly expressed in PBC specimens.

(A) Representative immunohistochemical staining in series sections of biopsied specimens from patients with primary biliary cholangitis (PBC). Immunohistochemical staining was positive for CK19, JCAD, and YAP in the portal triads from PBC patients compared to the normal control (NC). The image was taken at original magnification (200×). Scale bars = 100 μm. Red arrows: bile ducts.